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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,916	01/08/2002	Thomas W. Leonard	033218-016	4094

7590                    03/17/2003

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[REDACTED] EXAMINER

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[REDACTED] ART UNIT      [REDACTED] PAPER NUMBER

1616

DATE MAILED: 03/17/2003

5

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/041,916	LEONARD, THOMAS W.
	<b>Examiner</b>	<b>Art Unit</b>
	Barbara P. Badio, Ph.D.	1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

#### A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on \_\_\_\_\_.
  - 2a) This action is FINAL.                    2b) This action is non-final.
  - 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.
- Disposition of Claims**
- 4) Claim(s) 1-19 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
  - 5) Claim(s) \_\_\_\_\_ is/are allowed.
  - 6) Claim(s) 1-19 is/are rejected.
  - 7) Claim(s) \_\_\_\_\_ is/are objected to.
  - 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All
  - b) Some \*
  - c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
  - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>4</u> . | 6) <input type="checkbox"/> Other: _____                                    |

### First Office Action on the Merits

#### ***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

- w 2. Claims 2, 8, 14, 16 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The courts have interpreted 35 USC 112 to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph are summarized in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). These factors are the nature of the invention, the breadth of the claims, the state of the prior art, the predictability or unpredictability of the art, the amount of guidance or direction presented, the presence or absence of working examples, the relative skill in the art and the quantity of experimentation necessary.

The phrase "derivatives thereof" lacks enablement by the present specification. According to the present specification the phrase is intended to encompass "any compounds **derived from or related to** the estrogenic compounds named herein", and,

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thus the instant claims include a vast number of compounds. However, the present specification lacks working examples of compounds that might fall within the definition set forth within the instant specification. Because of the lack of guidance by the instant specification, the skilled artisan would be unable to practice the claimed invention because he would be unable to readily determine prior art compounds that fall within the definition set forth. In order to use the claimed invention commensurate in scope with the instant claim, the skilled art would have to first determine compounds that satisfy the definition of "derivatives" as defined by applicant. Said determination would result in undue experimentation.

It is suggested that said phrase be deleted from the instant claims.

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Raijmakers et al. ('639), Simoons ('820), Raveendranath et al. ('717), Shah et al. ('039), Bender et al. ('638) and Kong et al. ('778) in combination.

The claimed invention is a process for the production of a stable composition comprising a mixture of sulfated estrogens.

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Raijmakers et al. teach sulfatation of estrogen mixtures (see the entire article, especially Examples 12-14).

Simoons teaches a stabilized composition of estrogens utilizing Tris (see Examples I-V, especially col. 7, lines 27-40).

Raveendranath et al. teach a process for the production of alkali metal 8,9-dehydroestrone sulfate esters and the production of a stabilized composition with Tris (see the entire article, especially col. 1, lines 36-63). The reference teaches mixture of 8,9-dehydroestrone with sodium hydride, reaction with trimethylamine-sulfur trioxide and addition of Tris (see Examples 1-7).

Each of Shah et al., Bender et al. and Kong et al. teach the production of sulfate esters of estrogens by reaction with a sulfur trioxide complex, such as trimethylamine-sulfur trioxide or triethylamine-sulfur trioxide (see the entire article, especially Example 1, '039; Example 1, '638; col. 13, lines 35-43, and col. 14, lines 65-67, '778). Shah also teaches the production of sulfate ester of an estrogen by first mixing said compound with sodium hydride before reacting with a sulfur trioxide (see Example 1, Method A).

The sulfatation of estrogen mixture would have been obvious to the skilled artisan at the time of the invention because (a) sulfatation of alcohols such as sterols utilizing a sulfur trioxide complex is well known in the art as evident by the Raveendranath, Shah, Bender and Kong; (b) addition of a stabilizer such as Tris to estrogenic compositions is also well known in the art as evident by Simoons and Raveendranath and (c) the level of skill of the ordinary artisan in the art at the time of the invention. The ordinary artisan in the art at the time of the invention would have the

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reasonable expectation that any alcohol or salt thereof, either alone or in combination with other alcohols or salts of said alcohols, would undergo sulfatation in the presence of any sulfatation agent, including a sulfur trioxide complex. Based on the teachings of the references as discussed above and the level of skill of the ordinary artisan in the art at the time of the invention, the claimed process is *prima facie* obvious. The motivation to make a stabilized composition comprising sulfated estrogens is based on the knowledge in the art that compositions comprising a mixture of estrogenic sulfate esters are useful in hormone replacement therapy (see for example, '820, col. 1, lines 20-31).

#### ***Other Matters***

5. The telephonic restriction requirement made by Examiner Qazi and applicant's election and traversal are noted. Said restriction requirement is withdrawn.

#### ***Telephone Inquiry***

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Radio, Ph.D. whose telephone number is 703-308-4595. The examiner can normally be reached on M-F from 7:30am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

*Barbara P. Badio*  
Barbara P. Badio, Ph.D.  
Primary Examiner  
Art Unit 1616

BB

March 13, 2003